Supplemental Online Content

Berg DD, Jhund PS, Docherty KF, et al. Time to clinical benefit of dapagliflozin and significance of prior heart failure hospitalization in patients with heart failure with reduced ejection fraction. *JAMA Cardiol*. Published online February 17, 2021. doi:10.1001/jamacardio.2020.7585

This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. Effect of dapagliflozin on the primary efficacy outcome by timing of most recent heart failure hospitalization in relation to trial enrollment in patients with and without type 2 diabetes mellitus.

Most Recent HF Hospitalization	***Events (n)***	***Patients (N)***	***HR (95% CI) (Dapa vs. Pbo)***
Patients with Type 2 Diabetes Mellitus			
Never	219	1,090	0.94 (0.72-1.23)
>12 months	95	448	0.66 (0.43-0.99)
≤12 months	172	601	0.6 (0.44-0.81)
Patients without Type 2 Diabetes Mellitus			
Never	195	1,403	0.72 (0.54-0.96)
>12 months	78	502	0.84 (0.54-1.32)
≤12 months	129	700	0.68 (0.48-0.97)

The gradient of relative risk reduction with dapagliflozin was consistent in patients with and without type 2 diabetes mellitus (p-interaction = 0.41). CI, confidence interval; dapa, dapagliflozin; HF, heart failure; HR, hazard ratio; pbo, placebo.

eTable 2. Adverse events by timing of most recent heart failure hospitalization in relation to trial enrollment.

Adverse Event	Timing of HF hospitalization relative to enrollment					
	No prior HF hospitalization		>12 months		≤12 months	
	Dapagliflozin n=1,245	Placebo n=1,242	Dapagliflozin n=486	Placebo n=464	Dapagliflozin n=637	Placebo n=662
Any serious adverse event	429 (34.5)	486 (39.1)	194 (39.9)	192 (41.4)	272 (42.7)	316 (47.7)
Discontinuation of study drug due to adverse event	57 (4.6)	56 (4.5)	25 (5.1)	29 (6.2)	29 (4.6)	31 (4.7)
Volume depletion	86 (6.9)	95 (7.6)	42 (8.6)	31 (6.7)	50 (7.8)	36 (5.4)
Renal adverse event	69 (5.5)	85 (6.8)	33 (6.8)	38 (8.2)	51 (8.0)	47 (7.1)

The safety population included all patients who had undergone randomization and received at least one dose of dapagliflozin (n=2,368) or placebo (n=2,368). All p-values non-significant except for any serious adverse event in patients with no prior heart failure hospitalization (p=0.016). HF, heart failure.